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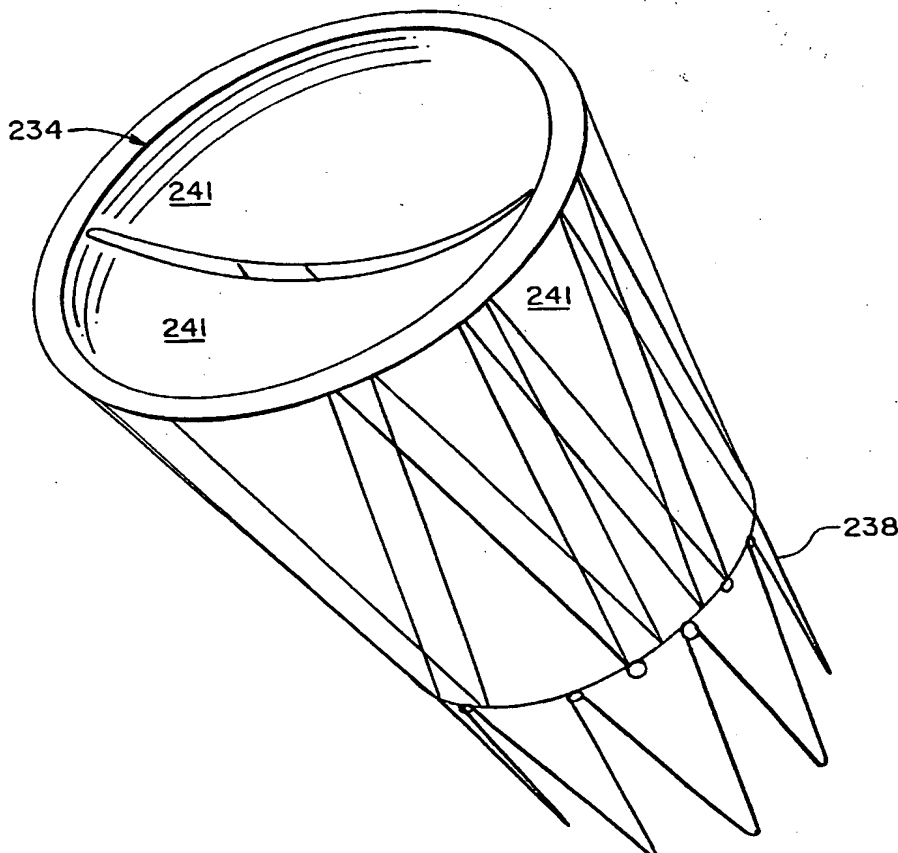
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[Continued on next page]

(54) Title: BULBOUS VALVE AND STENT FOR TREATING VASCULAR REFLUX



(57) Abstract: A stent and valve device (43) assembly for manufacture using suitable biocompatible materials and for placement, preferably percutaneously, into a vascular lumen.

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BULBOUS VALVE AND STENT FOR TREATING VASCULAR REFLUX

Field of the Invention

5 The present invention relates to venous valve replacement and, in particular, to replacement venous valves to lower extremities and a therapeutic method of treating venous circulatory disorders.

Background of the Invention

10 Chronic venous insufficiency (CVI) of the lower extremities is a common condition that is considered a serious public health and socioeconomic problem. In the United States, approximately two million workdays are lost each year, and over 2 million new cases of venous thrombosis are recorded each year. About 800,000 new cases of venous insufficiency
15 syndrome will also be recorded annually. Ambulatory care costs of about \$2,000, per patient, per month' contribute to the estimated U.S. cost of \$16,000,000 per month for the treatment of venous stasis ulcers related to CVI.

 It is estimated that greater than 3 % of the Medicare population is afflicted by a degree of CVI manifested as non-healing ulcers. Studies have indicated that about 40% of
20 seriously- affected individuals cannot work or even leave the house except to obtain medical care: It is estimated that 0.2% of the American work force is afflicted with CVI.

 Chronic venous insufficiency arises from long duration venous hypertension caused by-, valvular insufficiency and/or venous obstruction secondary to venous thrombosis. Other primary causes of CVI include varicosities of long duration, venous hypoplasia and
25 arteriovenous fistula: The signs and symptoms of CVI have been used to classify the degree of severity of the disease., and reporting standards have been published. Studies demonstrate that deterioration of venous hemodynamic status correlates with disease severity. Venous reflux, measured by ultrasound
 studies, is the method of choice of initial evaluation of patients with pain and/or swelling in
30 the lower extremities. In most serious cases of CVI, venous stasis ulcers are indicative of incompetent venous valves in all systems, including superficial, common, deep and communicating veins. This global involvement affects at least 30% of all cases. Standard principles of treatment are directed at elimination of venous reflux. Based on this observation, therapeutic intervention is best determined by evaluating the extent of valvular
35 incompetence, and the anatomical distribution of reflux. Valvular incompetence, a major

component of venous hypertension, is present in about 60% of patients with a clinical diagnosis of CVI.

Endovascular valve replacement refers to a new concept and new technology in the treatment of valvular reflux. The concept involves percutaneous insertion of the prosthetic device under fluoroscopic guidance. The device can be advanced to the desired intravascular location using guide wires and catheters. Deployment at a selected site can be accomplished to correct valvular incompetence. Percutaneous placement of a new valve apparatus provides a less invasive solution compared to surgical transposition or open repair of a valve.

The modern concept of a stent was introduced in the 1960s. Subsequently, it has been successfully incorporated in the treatment of arterioral aneurysms and occlusive disease. The use of endovascular stents represents one of the most significant changes in the field of vascular surgery since the introduction of surgical graft techniques in the early 1950s.

Initially, the dominant interest of vascular specialists was application of stents in the arterial system. The venous system and venous disease were not considered an arena for stent application. The utilization of endovascular treatment in venous disease was initially confined to the treatment of obstruction, in the pelvic veins [for CVI] as well as treatment of obstructed hemodialysis access grafts and decompression of portal hypertension (TIPS). Although these procedures enjoy widespread application, the actual number of patients involved is relatively low compared to the number afflicted with CVI and related syndrome. Thus, the necessity for therapy using endovascular technology for the treatment of venous disease arose. The prevalence of CVI and the magnitude of its impact demand development of an effective alternative therapy.

Brief Description of the Drawings

Figure 1 is a schematic representation of a portion of a venous system.

Figure 2 is a schematic representation of a section view of a portion of a venous system at a closed venous valve.

Figure 3 is a schematic representation of a sectional view of a portion of a venous system.

Figure 4 is a schematic representation of a portion of a venous system.

Figure 5 is a schematic representation of a section view of a portion of a venous system at an open venous valve.

Figure 6 is a schematic representation of a section view of a portion of a venous system showing a deployment system for a device of the invention.

Figure 7 is a schematic representation of a section view of a portion of a venous system showing a deployed device of the invention.

5 Figure 8 is a schematic view of one embodiment of the invention.

Figure 9 is a schematic view of one embodiment of the invention.

Figure 10 is a schematic view of one embodiment of the invention illustrating angular relationships of components.

Figure 11 is a top plan view taken along line 11-11 of Figure 9.

10 Figure 12 is a schematic elevation view of one embodiment of the invention.

Figure 13 is a schematic view of various valve material placement embodiments of the invention.

Figure 14 is a schematic view of a multiple stage embodiment of the invention.

15 Figure 15 is a side elevation view of a six strut dual stage embodiment of the invention.

Figure 16 is a side elevation view of a six strut dual stage truncated cone embodiment of the invention.

Figure 17 is a photo image of an embodiment of the invention in vivo.

Figure 18 is a photo image of an embodiment of the invention in vivo.

20 Figure 19 is a photo image of an embodiment of the invention in vivo.

Figure 20 is a photo image of an embodiment of the invention in vivo.

Figure 21 is a photo image of an embodiment of the invention in vivo.

Figure 22 is a photo image of an embodiment of the invention in vivo.

25 Figure 23 is a photo image of an embodiment of the invention in vivo. Figure 24 is a perspective view of one embodiment of the invention.

Figure 25 is a flow diagram depicting one embodiment of the invention.

Figure 26 is a flow diagram depicting one embodiment of the invention.

Figure 27 is a side elevation depiction of another embodiment of the invention.

Figure 28 is a representative sizing view of the invention according to Figure 27.

30

Summary of the Invention

A replacement valve assembly designed for optimized shaping and fit is provided that is configured for implantation within a vascular lumen. The valve assembly comprises a

plurality of flexible members, with each flexible member arranged to cooperate with at least one other flexible member to unidirectionally admit vascular fluid through the valve assembly. In one embodiment, at least a portion of one of the flexible members includes natural sclera tissue. In other embodiments, the flexible members include at least a portion of either SIS or other known biocompatible material. Methods of manufacturing the flexible members and of assembling and delivering the assembly to the patient's venous system are also provided.

Detailed Description of the Preferred Embodiments

Within the field of endovascular treatment, no previous technology has effectively combined a replacement valve and a stent in a percutaneously located assembly. Indeed, recognition of the need for such a device, system and method of employment has been lacking. Attempts at venous valve repair are not common. Indeed, minimally invasive repair or replacement procedures are quite uncommon. This is due, in part, to the poor availability of properly sized and properly designed prosthetic venous valves. United States Patent 5,500,014 has an excellent discussion of the different attempts to provide prosthetic venous valves, and such discussion is incorporated by reference herein. For the anatomy of venous valves, an excellent reference includes Venous Valves, by R.Gottlub and R.May, published by Springer Verlag, Austria, 1986.

The inventors have devised a device, system and method of deployment for a stent and valve assembly utilizing various materials having excellent cost, biocompatibility, and ease of use. In one embodiment, a stent is assembled having excellent length and stability characteristics, as well as an improved profile for ease of placement and automatic deployment at a deployment site. The assembly does not rely on placement at a previous valvular site but may be utilized either proximate or distal to the incompetent valve site due to the self-expanding features and improved anti-migration characteristics of the assembly.

The use of the material chosen for endovascular valve replacement in this assembly represents a unique application of a biocompatible substance. Whether the material is formed of elastomer, sclera, small intestine sub-mucosa (SIS), other mammalian tissue, or other suitable material, the venous stent device of this invention will serve as a substitute for deteriorated venous valves which have been altered by thrombosis or congenital hypoplasia. The valve prosthesis within the self-expanding stent will be percutaneously introduced with a small sized catheter delivery system. Justification for development of this invention is based

on the incidence of venous disorders that lack adequate endovascular therapy. Patients who are treated surgically undergo a more invasive method that involves greater costs and more numerous potential complications. The minimally invasive technique of this invention will decrease length of hospital stay, lower over-all costs and permit an almost immediate return to normal activity. Indeed, it is believed that the availability of this treatment will dramatically alter the lives of many people, including those who might not have been able to undergo previous surgical techniques for the repair or replacement of damaged venous valves.

Figure 1 is a schematic representation of an exemplary portion 10 of a human venous system. In venous system portion 10, a representative venous valve 15 is illustrated and shown in a closed position. As is well understood, the flow of blood through venous system 10 is in the direction of arrows 17, with the dominant pressure illustrated by a symbol P_1 . Although the venous system is designed to ensure flow of blood from extremities back to the heart, Figure 1 also illustrates the phenomenon of retrograde flow and retrograde pressure which exists in the venous system and which is illustrated by symbol P_2 . The design of competent human venous valves takes into account this retrograde pressure. Accordingly, the configuration of bicuspid venous valve 15 accommodates the pooling of the blood at a plurality of sites each known as a valvular sinus 22. The temporal pooling of blood in each sinus or pocket creates retrograde pressure against the valve leaflets and facilitates closure of the free borders 27 of the valve cusp. Although the clear majority of human venous valves are of the bicuspid variety, it is noted that certain venous valve formations in humans may also include other than bicuspid configurations.

Figure 2 is a sectional view taken along line 2-2 of Figure 1. In Figure 2 it may be seen that the free borders 27 of cusp 29 of valve 15 are essentially closed, and are facilitated in maintaining that closure by the pressure of blood pooling in the valvular sinus areas 22. It is recognized that the free borders 27 of the valve cusp may actually present as an undulating shape rather than merely a substantially straight shape across the diameter of the valve when viewed from section A as shown in the healthy venous valve schematically represented in Figure 3, the vertical length L of valve 15 cusp 29 is often at least about twice the diameter d of the respective blood vessel. This relationship, though not absolute, is quite common. Also, the free borders 27 of the valvular cusps of bicuspid valve 15, when closed, may contact each other over a length corresponding to approximately $1/5$ to $1/2$ of the venous diameter d at the site of the particular valve. Thus, the natural human bicuspid venous valve, in a competent

state, utilizes both the axial and retrograde pressure of the blood in the valvular sinus, as well as the contact of the lengthy free ends of the valve cusps to maintain closure. In other words, the contact of the free ends is further enhanced by the axial pressure created by the weight and volume of the pooled blood in the sinus areas.

5 Replication of this phenomenon has generally been beyond the technical ability of known devices or prostheses. The challenge is particularly formidable in view of the anatomy of the venous valve system and in particular the nature of veins themselves. One example of the challenge attendant to venous valve replacement relates to the shape of the veins in the venous system. Indeed, inside the body, veins will have cross-sections of elliptic shape,
10 particularly at the venous valve locations. This is due to the interaction of the skin, the subcutaneous fascia, and other tissue that presses the veins toward the muscles, or the muscles pressing the veins toward the bone. This results in the free ends of the valvular cusps being generally aligned along the longitudinal axis of the above-described ellipse. Therefore, proper insertion of or repair to venous valves involves precise orientation within the vessel.
15 As appreciated from the above description, the optimum apposition of the free ends of venous valve cusps is achieved when the valvular cusps are aligned with the longest diameter of the ellipse. The venous system also includes, as shown in Figure 3, a slight thickening of the vessel wall proximate each venous valve. Figure 4 illustrates venous system portion 10, corresponding to that shown in Figure 1, but with venous valve 15 in an open configuration
20 and normal blood flow proceeding through the valve. Figure 5 illustrates, similar to Figure 2, the action of the free ends 27 of valve 15 cusps.

Figure 6 illustrates one embodiment of a deployment technique for deploying a valve and stent into a venous system according to the invention. In this figure, catheter means 38
comprises a portion of an interventional system facilitating, through various guiding
25 technologies, placement and deployment of a stent and valve device 43 at an optimum location within representative venous system 10. It is understood that the optimum location for placement of stent and valve device 43 is generally proximate to existing sites of venous valves in the patient receiving the stent and valve device. However, it is recognized that by using the teachings of this invention it is possible to further optimize and possibly customize
30 a stent and valve device 43 suitable for placement at various locations according to the anatomy of the patient's vein at the specific locations. Further discussion of this feature of the invention is included below. Figure 6 illustrates the stent and valve device 43, with the stent portion partially deployed from the catheter means 38.

Figure 7 is a representative, schematic, illustration of a venous portion 10, as shown in Figure 6, with a fully deployed stent and valve device 43 therein. In this embodiment, the stent portion 51 of stent and valve device 43 comprises a functionally unitary mesh-type construction. As is understood in the art, stent material may vary according to the lumen or other tissue structure for which it is designed to provide support. In this instance, stent portion 51 accommodates the inner lumen of venous portion 10 sufficient to allow valve portion 55 sufficient diameter to properly function as an artificial venous valve. In Figure 7, valve portion 55 is shown in a closed position. However, the inventors have discovered certain optimal features and properties for stent and valve device 43, which although they may vary according to design and patient need, may represent further improvements over the embodiment illustrated in Figure 7.

The size of a preferred stent and valve device 43 is determined primarily by the diameter of the vessel lumen (preferably for a healthy valve/lumen combination) at the intended implant site, as well as the desired length of the overall stent and valve device. This latter feature is for optimum placement by achieving the best stability during the employment. Thus, an initial assessment of the location of the natural venous valves in the patient is determinative of several aspects of the prosthetic design. For example, the location will determine the number of support struts, the type of valve material selected, the size of deployment vehicle (French size of catheter or other deployment means) and the characteristics of the valvular sinus-like pockets. These and other factors must be considered according to the patient need. In one embodiment, the inventors have utilized algorithmic means for determining proper fit and customization of valves suitable for replacement of incompetent or insufficient valves in the patient. Once again, further discussion of this method is discussed herein below.

Another representative stent and valve device is shown in Figure 8. In this embodiment, the stent and valve device 61 is simplified to demonstrate the 4-point connection of the selected valve material 73 at connection sites 80 on stent frame 84. Once again, stent frame 84 is shown in very simplified form but is adequate to demonstrate the challenge of having only a very minimum number of connection sites 80. This is challenging because it is important that the valvular sinuses retain the blood above the valve when the valve is in the closed position. Otherwise, a condition known as reflux exists. Obviously, a single point connection to the stent frame portion adjacent the luminal wall probably will not provide adequate sealing of the valve material to the wall to prevent retrograde flow of blood

past the valve. Indeed, what has been determined is the need for multiple point connection of the valve material to the stent structure to properly emulate the natural competent valve.

Referring to Figures 9 and 10, an exemplary single-stage stent and valve device, referred to in this embodiment as device 86, comprises multiple connection points 91 for the selected valve material 89 along various struts 93 of stent frame structure 95. The number of struts may vary between merely several struts to upwards of eight to ten struts or even more, as appropriate, according to the lumen size of the vein. For example, in the embodiment of Figure 9, using valve material comprising either naturally occurring sclera tissue or naturally occurring small intestine sub-mucosa (SIS) or other comparable materials, or a combination thereof, it is possible to utilize between about six to twelve struts and deploy the stent and valve device 86 utilizing an approximately ten to fourteen French deployment catheter system.

Another consideration in the design and construction of stent and valve device 86 relates to the angle at which the valve material extends from the circumferential wall, i.e., the inner venous wall. In Figure 10, a partial stent frame structure is shown as a vertical wall strut 101 corresponding to the elastic membrane and endothelial cells of the inner wall of a venous blood vessel. Valve material 105 is shown extending from a portion of strut 101 with a first side 107 corresponding to the luminal part facing the lumen of the vessel and a parietal part 109 facing the wall of the vessel. Thus, the angle formed between strut 101 (corresponding to the venous wall) and valve material 105 is defined as angle V as shown in Figure 10. The normal flow of blood through the stent and valve device 86 in the embodiment depicted in Figure 10 is in the direction of arrow F. Thus the angle V corresponds to the angle at which the venous valve structure extends from the luminal wall of a natural venous valve. Although various connection angles occur, it is believed that in the region of the natural valvular agger connection area (corresponding to area 113 of Figure 10) angle V is in a range of between about 35° to 70°. It should also be recognized that the luminal part of a natural venous valve in a human patient comprises a plurality of crypt-like crevices that further provide means for capturing and collecting the blood pooling in the valvular sinus areas. These crypts do not occur on the parietal side of the valve. Thus, in addition to whatever angle is selected for an artificially manufactured venous valve, it is important to note that there is no disclosure in any known prior artificial valve system to accommodate the angle V and the crypt structure. However, to the extent that a naturally occurring and non-thrombolytic substance may be used for valve material, it is possible that the structure may include substructures that act

similar to the collection features of the naturally occurring crypts. For example, if valve material 105 is manufactured utilizing natural tissue such as the above-referenced SIS or sclera tissue, rather than a plastic or elastomer material, then the increased benefits of the tissue structure acting as pseudo-crypts may in fact provide unrealized advantages in a venous valve structure. It should also be appreciated that such advantage may be more accurately emulated subject to the cost limitations and manufacturing techniques attendant to manufacture of inventions disclosed herein. It is worth noting that this and other features of the invention may also be appropriate for placement into a non-venous valve device. Figure 11 illustrates a top plan view of Figure 9, in which the points of attachment are indicated and the free ends 27 of the valve material cusps are shown in apposition.

Figures 12 and 13 illustrate the optional radius R which may be formed at the free ends 27 of the valve material 89. A certain amount of radius allows improved functionality for a valve and stent device, subject to the size of the device and the location of use. Figure 13 also indicates several options for attachment locations for free ends 27 on stent frame members. Any of these options may be selected, although a preferred embodiment may also be selected from other figures herein. It is noted that for certain uses valvular sinuses may be either deep or shallow, and the free ends of the valve material may be either centered or offset from a diameter when attached to the stent frame struts or other structure.

Figure 14 illustrates another embodiment of stent and valve device 133 of the invention. The inventors realized that during deployment, under certain conditions, the self-expanding frame structure 137 and marginal retaining members 140 are inadequate to prevent momentary lack of control. As shown, frame structure 137 will expand and contract according to the pressure applied to the frame in axial directions, as shown by symbols E and C in Figure 14. In particular, when a single stack device is allowed to exit or otherwise be liberated from a deployment means, the device may expand at an undesired rate. This may result in lack of stability during and after deployment. In order to overcome this concern, a double stacked device 133 is provided. As shown, device 133 is configured with valve material 146 arranged so that free ends 153 are proximate an end 149 of the device, rather than lower within the volume of the device. As noted in relation to Figure 13, it is possible within the scope of this invention to alter the location of the valve material, as appropriate. The double stack feature of this device allows for deployment of one stack, and engagement and stability of the deployed stack to occur prior to liberating the second stack. However, the

second stack is held in place pre-liberation by the deployment means, e.g. a catheter deployment means.

Figures 15 and 16 illustrate further embodiments of a stent and valve device 167, similar to that shown in Figure 14, but having only six struts 174 per stack or stage. These devices are configured with marginal wires or other thin retaining means 181 providing connection through eye-loops 184 on each strut. The truncated cone arrangement of Figure 16 may be particularly useful in certain geometries of vein locations. Figures 15 and 16 each disclose an excellent embodiment for employment as a modular design for controlled deployment. Indeed, such a design as shown in Figure 15 has been tested in vivo, with excellent results for stability and valve operation.

Example 1

Figure 17 is an in vivo photo image taken of porcine subject #5020 with the Emitron Corporation DigiMed IITM imaging system of a venous system portion in which a device according to the invention is being deployed. Stent and valve device 202 is shown in its compressed configuration within the deployment catheter. Device 202 is approximately 2 cm in length, and is about 15 mm in fully extended diameter. In this example, valve material comprising SIS is used, although sclera was used successfully in similar trials. Figure 18 shows device 202 having deployed first stage 205 to establish a stable platform, and second stage 208 (with the valve material therein) in the process of deployment. Figure 19 shows the fully expanded device 202 which has accommodated the internal lumen of the venous site and has placed the valve material in position. Figure 20 is a further view of device 202 during the systolic flow of blood through the device 202, and with the imaging system measuring gage 213 shown in a verification mode to ensure proper deployment. Verification of valve functionality is also shown in Figure 21. In that Figure, the venous portion is shown in diastole, with the blood pooled in valvular sinus areas 220 and 221 (partially hidden due to orientation of image). Figure 21 clearly illustrates the anti retrograde feature of device 202 according to several of the teachings of the invention.

Example 2

Figure 22 is an in vivo photo image taken of porcine subject #5022 with the Emitron Corporation DigiMed IITM imaging system of a venous system portion in which a device according to the invention is being deployed. Stent and valve device 202 is shown in its

partially deployed configuration within the deployment catheter. Device 202 is approximately 2 cm in length, and is about 15 mm in fully extended diameter. In this example, valve material comprising SIS is used, although sclera was used successfully in similar trials. Figure 22 shows device 202 having deployed first stage 205 to establish a stable platform, and second stage 208 (with the valve material therein) in the process of deployment. Figure 23 shows the fully expanded device 202 which has accommodated the internal lumen of the venous site and has placed the valve material in position. Verification of valve functionality was demonstrated in similar manner to that shown in Figures 20 and 21 of Example 1.

10 Example 3

The feasibility of a stent-valve combination was studied in the laboratory and in a porcine model. A modified self-expanding stent was combined with a biocompatible material to assess the efficacy, thrombogenicity and histocompatibility of a new prosthesis. The material was configured in a spherical shape and fashioned into adjacent leaflets as a bi-valve design. Leaflets were secured to the stent with 7-0 nylon interrupted sutures. Hydrodynamic and barometric tests were conducted in clear tubular apparatus with variable pulsatile flow. Upon confirmation of valvular integrity, a pilot animal study was conducted. Under general anesthesia, prostheses having a tradename of Valvestent™ were implanted, from a jugular approach, in the distal IVC of 4 six-month old swine. Animals were maintained on warfarin anticoagulant to reduce the risk of embolism.

Following a 30-day observation, with no mortality or extremity edema, a second set of 14 swine underwent baseline phlebography and Valvestent™ prosthesis placement. Follow-up studies were performed at 30, 60 and 180 days consist of phlebography, perfusion retrieval of IVC and iliac veins for histological analysis, and autopsy examination for pulmonary embolus.

Initial hemodynamic testing revealed 10-20% reflux, which was corrected with design modifications. The valve opens with low pressure and maintains shape with elevated hydrostatic pressure above. All animals rapidly recovered from the implantation procedure with no ill effects. Thirty-day mortality is 78% (14/18). One animal died of malignant hyperthermia during surgery, and three animals died at 6-8 days due to internal bleeding

related to prolonged prothrombine time. Primary patency of the prostheses at 30 days is 100%. One pilot stent migrated to the pulmonary artery, but remained patent.

5 The combination of a self-expanding stent and biocompatible material suitable for formation of durable, flexible and non-thrombogenic valve substitute, which does not reflux, appears feasible. Percutaneous delivery of such a ValvestentTM prosthesis assembly would permit a minimally invasive treatment for lower extremity valvular insufficiency.

10 Figure 24 illustrates an alternate embodiment stent and valve device 234. Device 234 has a two stage stent 238 configuration, with valve material 241 arranged both inside the lumen and outside the structure of the generally tubular shaped device. This example is of a relatively shallow sinus variety, and may be one of several embodiments which have dual application to both venous and other vascular uses, including, e.g., an arterial-venous fistula treatment device.

15 Figure 25 is a flow diagram of a method of configuring a sheet or other portion of valve material for use in stent and valve devices according to the various embodiments of this invention. Block 263 illustrates obtaining basic tissue or other suitable material for use as valve material and providing it in a generally planar form 266 for later processing. In block 272, the material is further shaped over convex/concave shaping means to provide optimum
20 concavity for use in the appropriately sized and shaped valvular sinus configuration. The final shaping and cutting is performed in block 279 at which the precise shape for use in a valve material leaflet is accomplished, including a plurality of arcuate and possibly other edge portions. As disclosed herein, various forms of sclera may be used in the embodiments of this invention. It has excellent features in most respects and is readily harvested at very low cost.
25 Also discussed herein is the use of the known material made of small intestine sub-mucosa, also referred to as SIS. Examples of this material, though not in this use and application, are found in United States Patents No. 4,902,508, 4,956,178, 5,516,533 and 5,641,518, each of which is incorporated herein by reference for the teachings of SIS related manufacture and principles of use.

30 Figure 26 illustrates an optional technique of manufacturing the proper stent and valve device of this invention according to its intended placement in a specific patient. In this technique, it is possible to utilize either some or all steps. In a full utilization of this methodology, a patient is designated 301 for sizing. The insufficient or incompetent valve

site or sites are identified 305 using imaging means, such as that identified herein or other systems having highly accurate capabilities. Sizing values for optimum stent and valve configurations are obtained 308 using the imaging means, and the values are then either stored or otherwise transferred 311 to stent and valve device manufacturing means. Molds or other tools may be effectively utilized in this process. In order to further customize or render more effective in some manner the manufacture of the valve material, it is desired to either select or obtain 315 a tissue sample from the patient or an appropriate subject. The tissue sample may then be utilized in known manner to construct or grow 319 a customized valve portion or portions for later use by the designated patient. Teaching examples of this tissue engineering technology are found in United States Patent Nos. 4,996,154, 5,326,357, 5,902,741, and 5,902,829, all of which are incorporated herein by reference for such teachings. Following proper growth of the valve material, the material is then assembled 323 with a properly sized stent, and then placed 327 in the patient at the specifically targeted site. A regimen of monitoring and follow up 331 continues as appropriate. It is believed that the teachings of this method of manufacture and use of the devices herein will greatly facilitate the treatment of many people for a medical problem of great severity and which little history of remedy.

Figure 27 illustrates yet another advancement in design stents according to the principles of the invention. As discussed above, the proper placement and accommodation of a replacement venous valve is enhanced by use of valves which are matched to each patient's physiology. Figure 27 shows one embodiment of stent and valve device 411 having a compound diameter with a first region L1 having a length corresponding generally to that depicted in Figure 3 as the customized length of the specific human valve cusp area. Region L1 has, in this embodiment, a varying diameter bulbous -shape formed by struts 419 of frame structure 425. It is appreciated that Figure 27 illustrates a portion of the valve schematically, and that the shape depicted will be arrayed fully about the circumference of the device. Second portions L2 are sized and designed using the fit and customization techniques herein to contact those portions of the inner lumen of the vein adjacent the primary valve implant site.

Figure 28 is a representative sizing example of a stent and valve device according to the embodiment shown in Figure 27. It is recognized that each human valve is different, and thus the importance of this invention, but this example shows one type of ratios useful for shaping the optimum frame structure. As shown, Figure 28 corresponds to Figure 27, and is

a side elevation view with D1 about 1.0 cm, D2 about 1.25 cm, H1 about 1.25 cm, and H2 about 2.0 cm.

The valves for placement within the frame structures of Figures 27 and 28 may be made from any known technique, although a preferred structure or mode of valve construction and assembly is as shown throughout this entire disclosure.

Because numerous modifications may be made of this invention without departing from the spirit thereof, the scope of the invention is not to be limited to the embodiments illustrated and described. Rather, the scope of the invention is to be determined by appended claims and their equivalents.

WHAT IS CLAIMED IS:

1. A self-expanding replacement valve assembly having a bulbous-shaped portion and which is configured for implantation within an avascular lumen, the valve assembly comprising
5 a plurality of flexible members, each flexible member conformed to cooperate with at least one other flexible member to unidirectionally admit vascular fluid through the valve assembly and to prevent retrograde flow of the vascular fluid through the valve assembly.
2. The assembly of claim 1, wherein at least a portion of one of said flexible members
10 includes either sclera or small intestine sub-mucosa material.
3. The assembly of claim 1, in which the flexible members are supported by flexible and resilient struts configured for use in a vascular lumen.
- 15 4. The assembly of claim 3, in which the struts are manufactured with a resilient metallic material.
5. The assembly of claim 4, in which the struts material is selected from either nitinol or stainless steel.
20
6. The assembly of claim 3, in which the struts are manufactured from a biodegradable-like material designed to dissolve in a patient after a certain period of time.
7. The assembly of claim 3, in which the flexible members are cusps of a valve having
25 edge portions configured for attachment to the struts, and edge portions configured to form free ends capable of reshaping to selectively form an opening through the valve assembly or an obstruction in the valve assembly.
8. The assembly of claim 1, in which the flexible members are bicusps.
- 30 9. The assembly of claim 1, in which the flexible members generally semi-elliptical in shape.

10. The assembly of claim 1, shaped as a generally tubular flexible member conformed to be implanted in a venous lumen in a fixed location.

11. The assembly of claim 3, in which the struts are connected to form a tubular shape and are flexible in a direction generally transverse to a longitudinal axis of the tubular shape, the flexible members being operably disposed in the tubular member.

12. The assembly of claim 11, in which each flexible member defines a first edge portion conformable to said tubular member and a second edge portion, the second edge portion of each flexible member cooperating to enable said unidirectional flow by forming a plurality of free ends which selectively engage and disengage each other.

13. A stent and valve assembly for use in a vascular lumen, comprising:

- a. a flexible and resilient structure of a plurality of struts designed as a variably diametered tubular shape; and
- b. a plurality of valve leaflets formed from either SIS or sclera material and attached along designated edge portions to a plurality of said struts to enable opening and closing of free edge portions to emulate the operation of a naturally occurring vascular valve.

14. The assembly of claim 13, having a two stage design of at least six struts in each stage.

15. The assembly of claim 13, in which the total length of the assembly is between about 1 and 2 cm, and the diameter of any stage is between about 8-20 mm.

16. A method of making a replacement valve assembly for implantation into a vascular lumen and to function as a check valve, the valve assembly comprising a plurality of flexible members, each flexible member conformed to cooperate with the other at least one flexible member to unidirectionally admit vascular fluid through the valve assembly, the method comprising the steps of:

- providing a flexible biocompatible material;
- constructing a plurality of flexible members from the flexible material; and

disposing the flexible members in a bulbous-shaped portion of a tubular member having at least one stage so as to function as a unidirectional flow valve.

17. The method of claim 16, in which sclera or SIS material is provided as the flexible material.

18. The method of claim 17, in which the tubular member is constructed as a two stage member to enhance stability during employment in a vascular lumen.

19. A method of treating chronic vascular insufficiency, the method comprising the steps of providing a replacement valve assembly shaped with a bulbous portion for implantation within a venous lumen, the valve assembly comprising a plurality of flexible members, each flexible member shaped to cooperate with the other at least one flexible member to unidirectionally admit vascular fluid through the valve assembly;

introducing at least one of said replacement valve assemblies into a venous lumen generally proximate an insufficient vascular valve; and fixing said replacement valve assembly in said venous lumen by actuating a self expanding portion of the valve assembly to engage the inner luminal wall of the venous lumen.

20. The method of claim 19, in which the replacement valve assembly is introduced into the venous lumen percutaneously.

21. The method of claim 20, in which the replacement valve assembly is introduced into the vascular lumen by a catheter with the replacement valve assembly within the catheter.

22. The method of claim 19, in which the venous replacement valve is made, at least partially, from mammalian tissue.

23. A method of making a vascular valve member assembly from mammalian sclera or small intestine sub-mucosa (SIS), the method comprising the steps of providing a mammalian tissue source; removing said tissue from the tissue source; and fashioning the valve member from the sclera or SIS.

24. The method of claim 23, in which a plurality of the valve members are attached at least in part to an inner portion of a self-expanding and generally tubular shaped strut assembly.

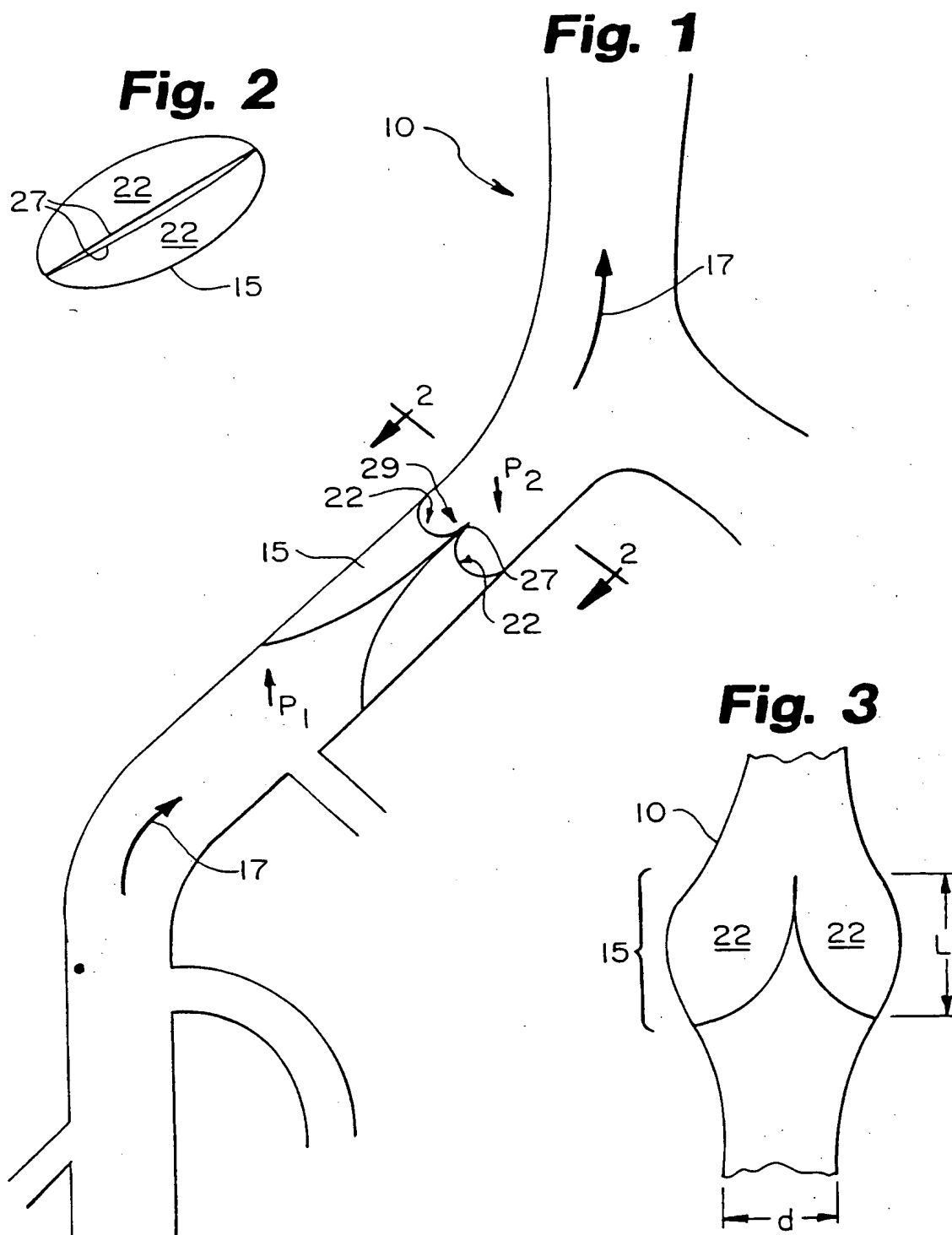
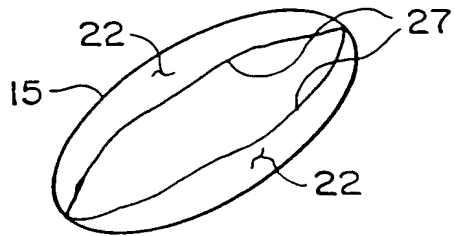
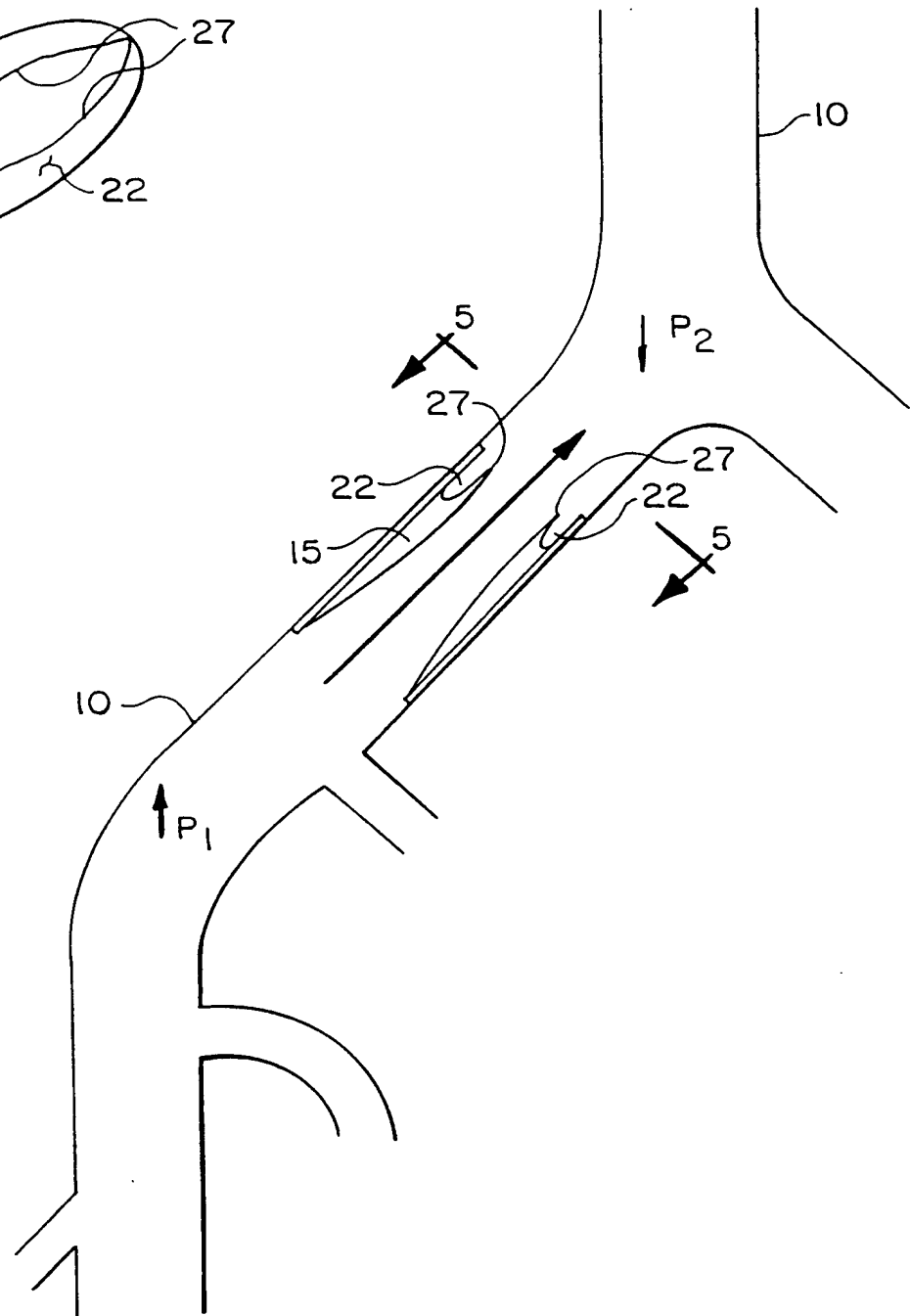
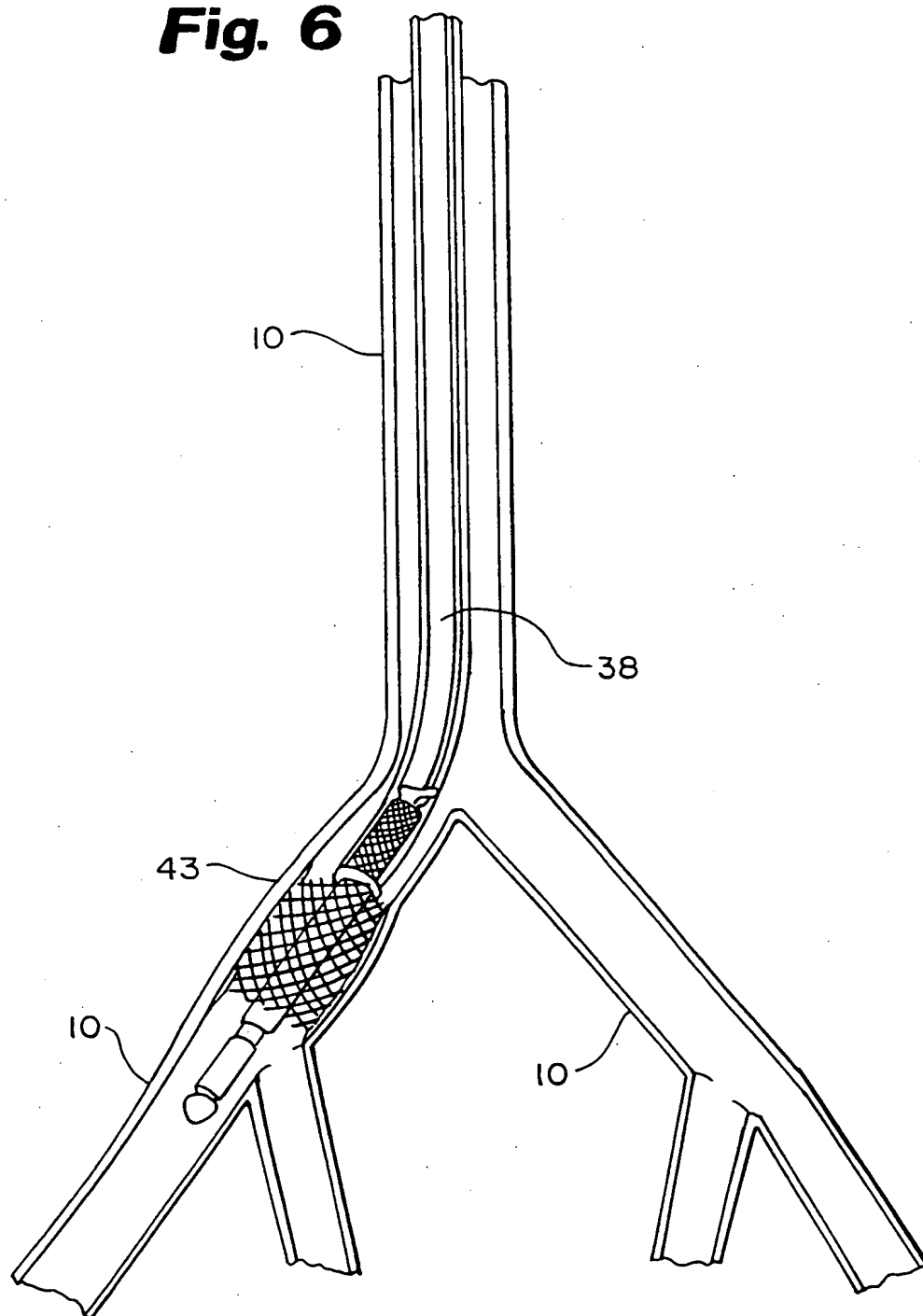


Fig. 5**Fig. 4**

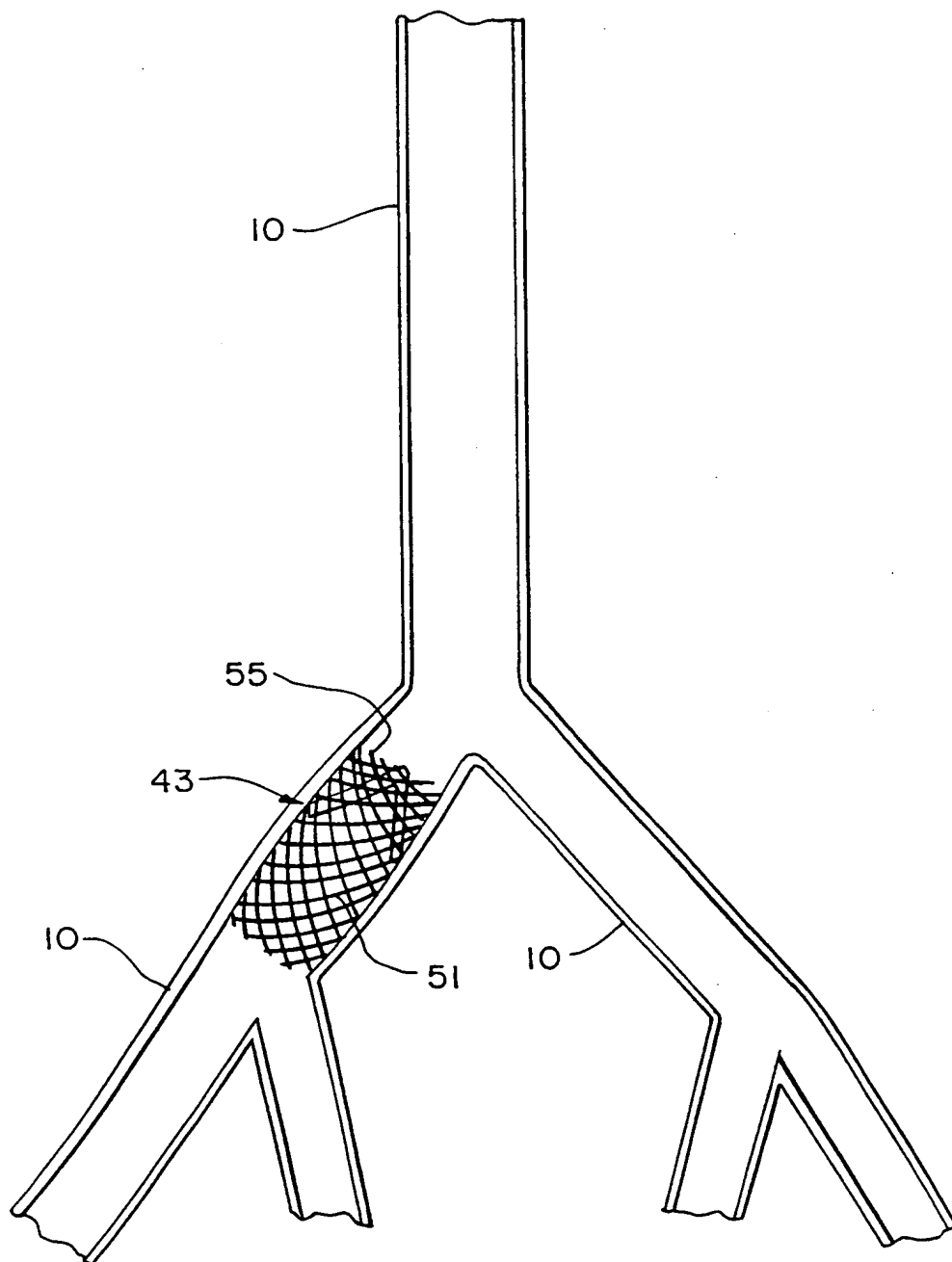
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Fig. 6

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Fig. 7



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Fig. 8

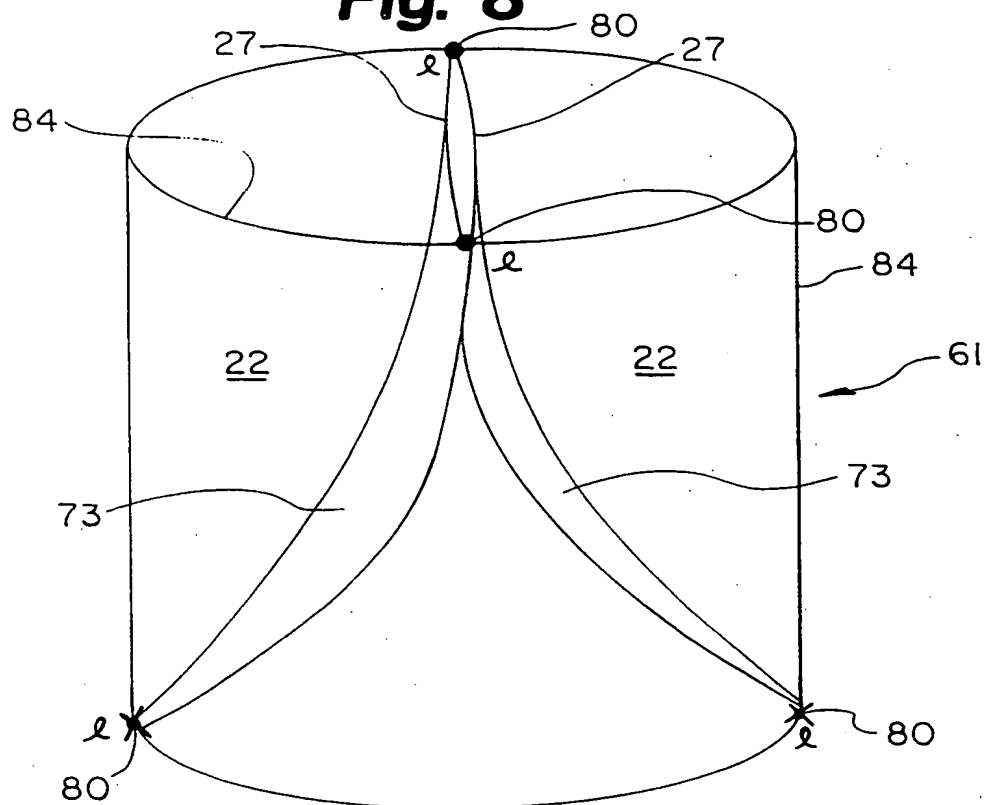
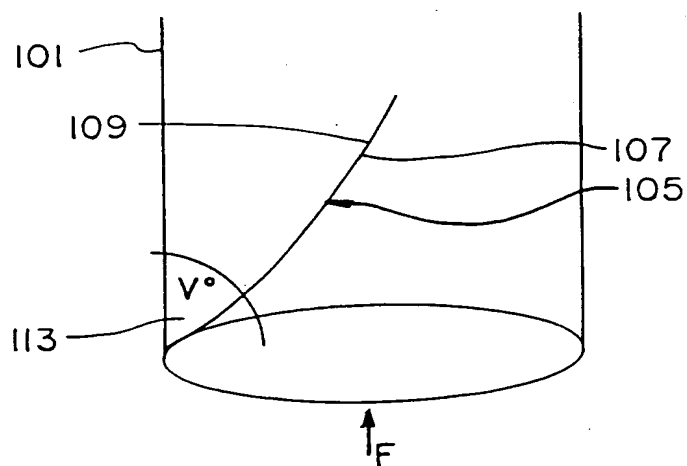


Fig. 10



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Fig. 9

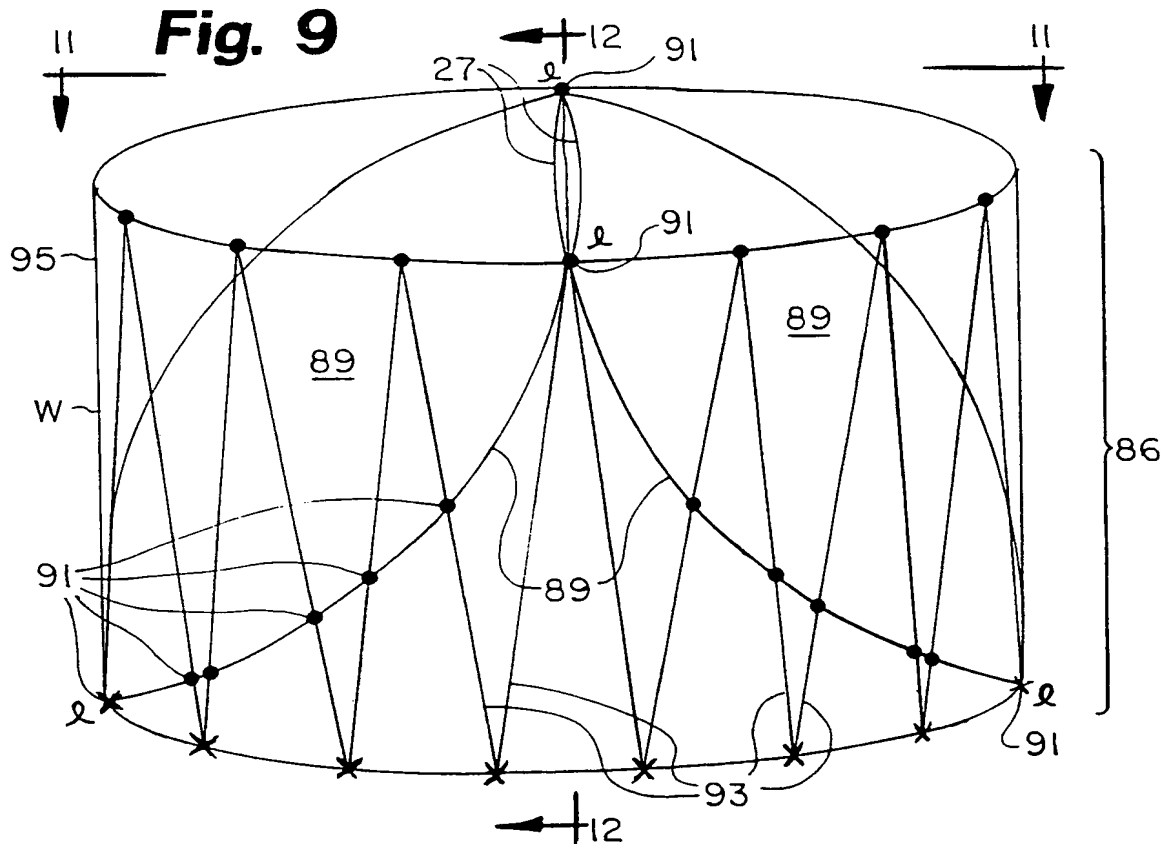
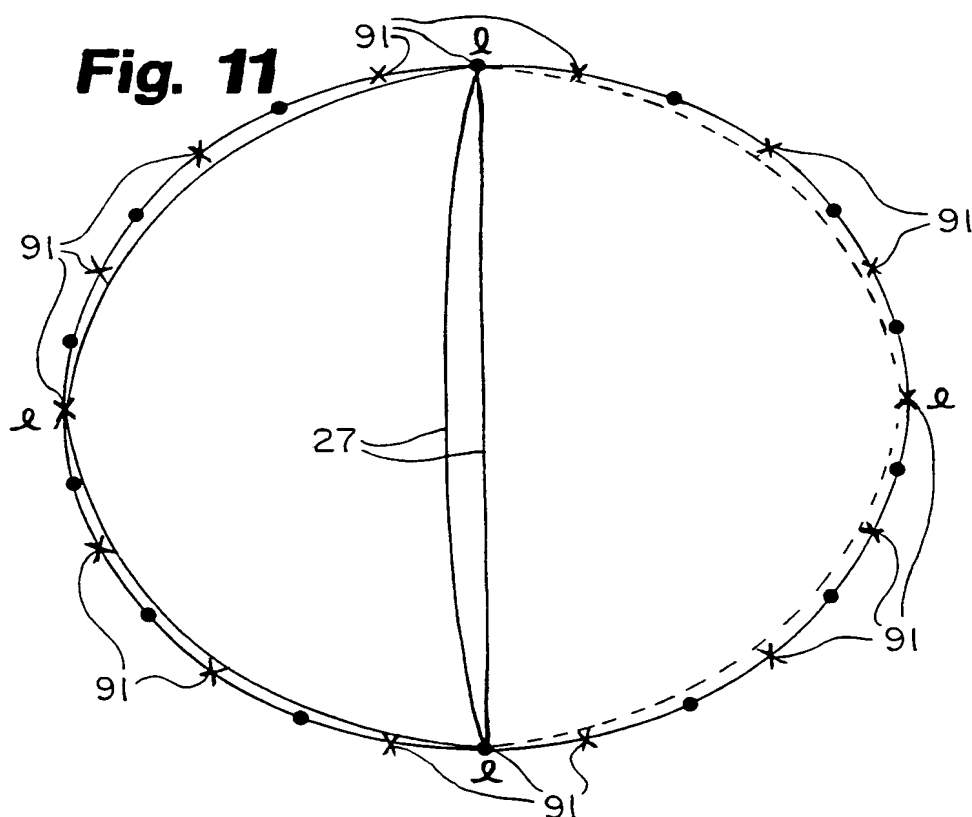


Fig. 11



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Fig. 12

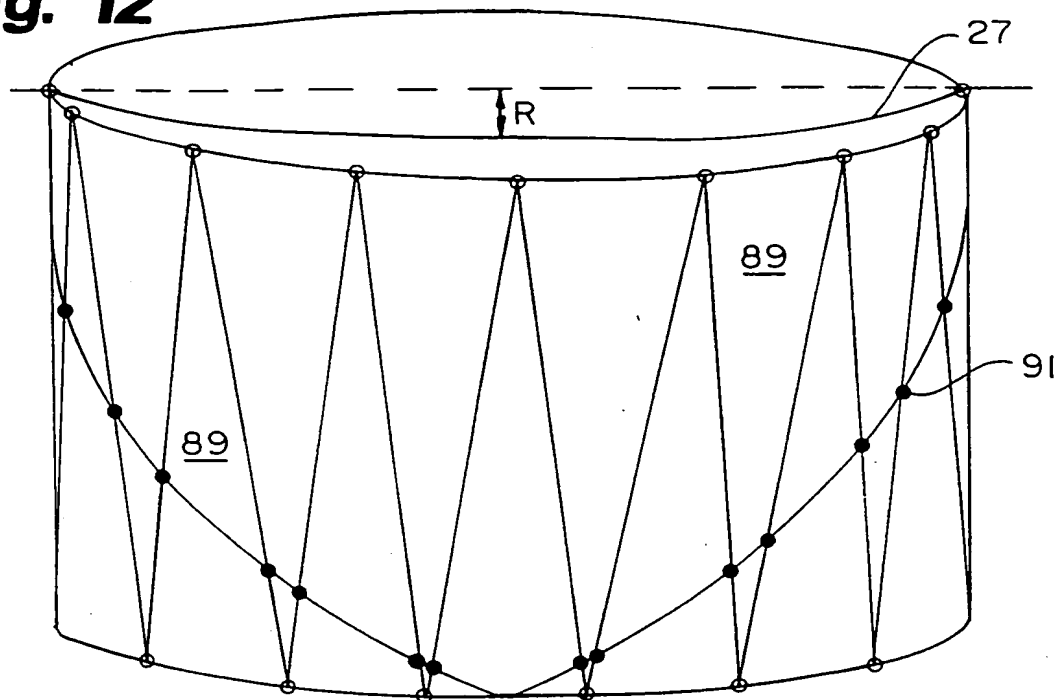
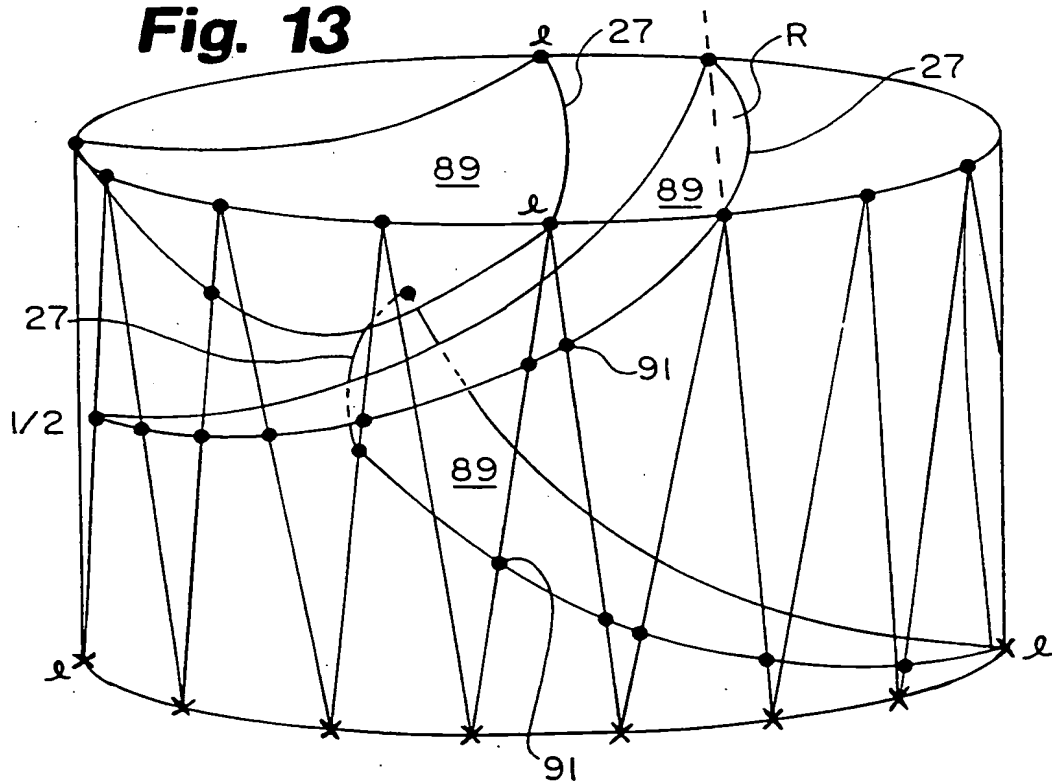
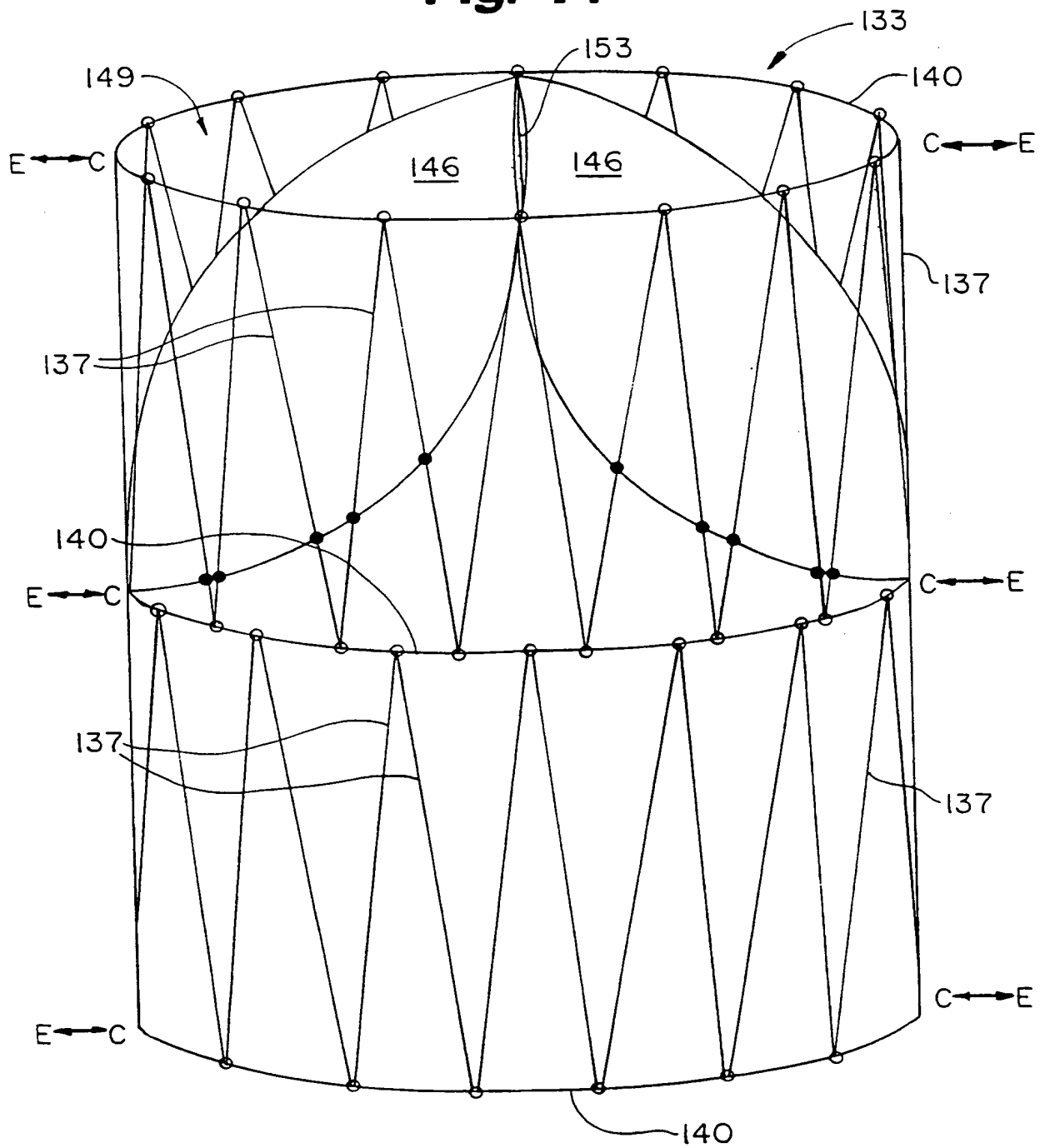


Fig. 13



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Fig. 14

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Fig. 15

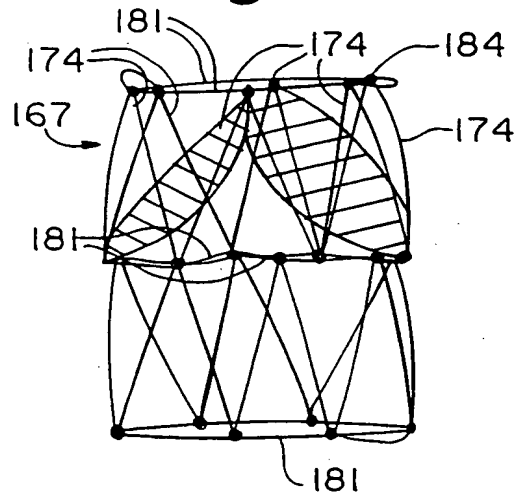
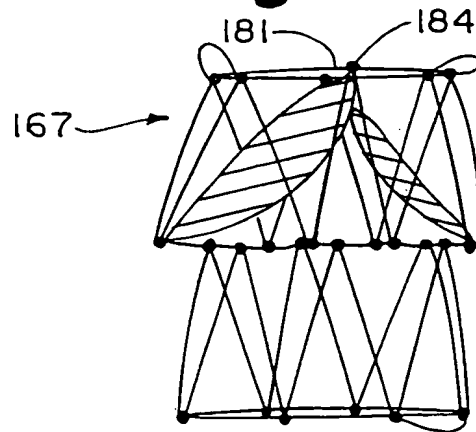


Fig. 16



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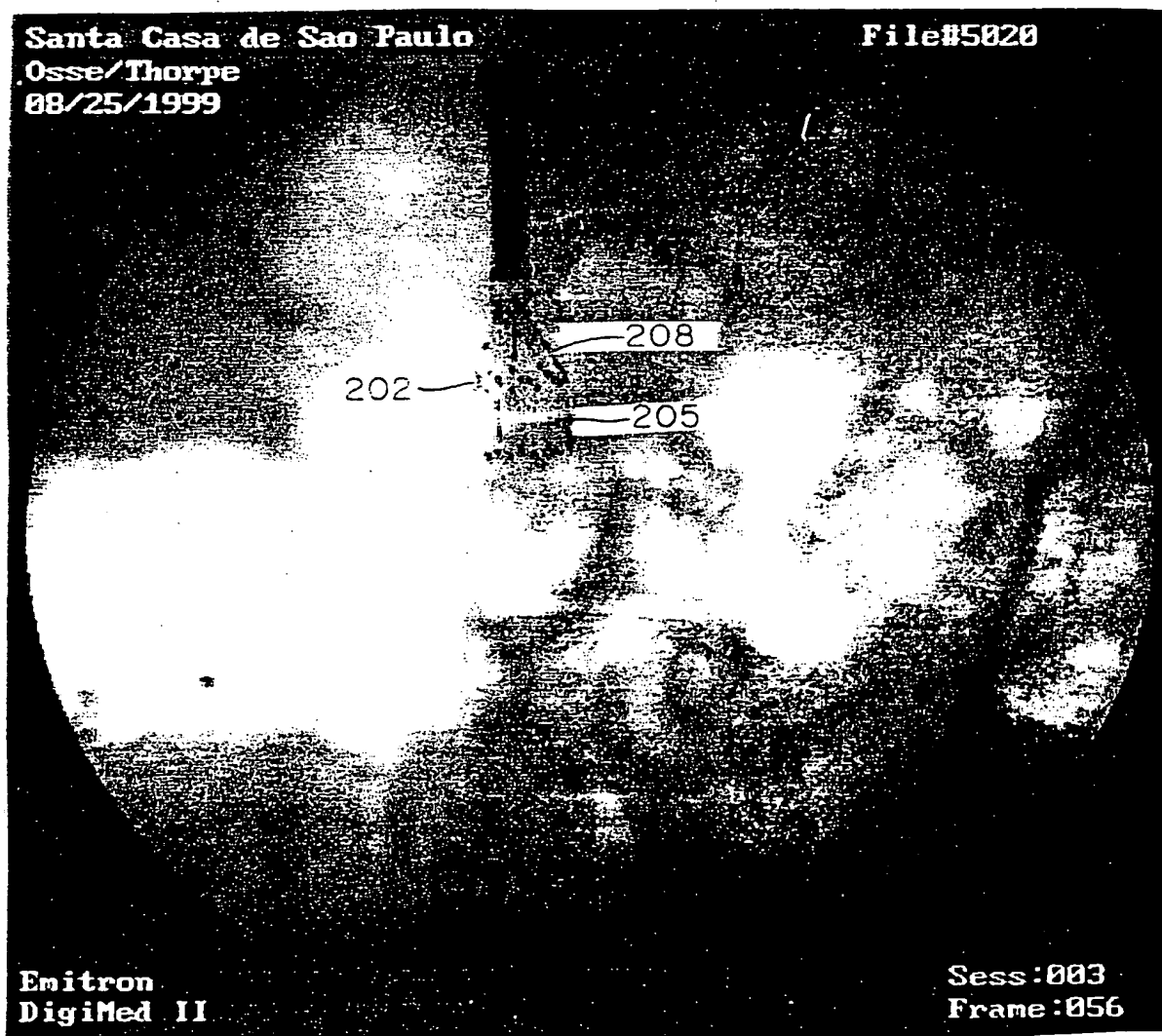
Fig. 17



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Fig. 18



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Fig. 19



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Fig. 20



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Fig. 21



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Fig. 22

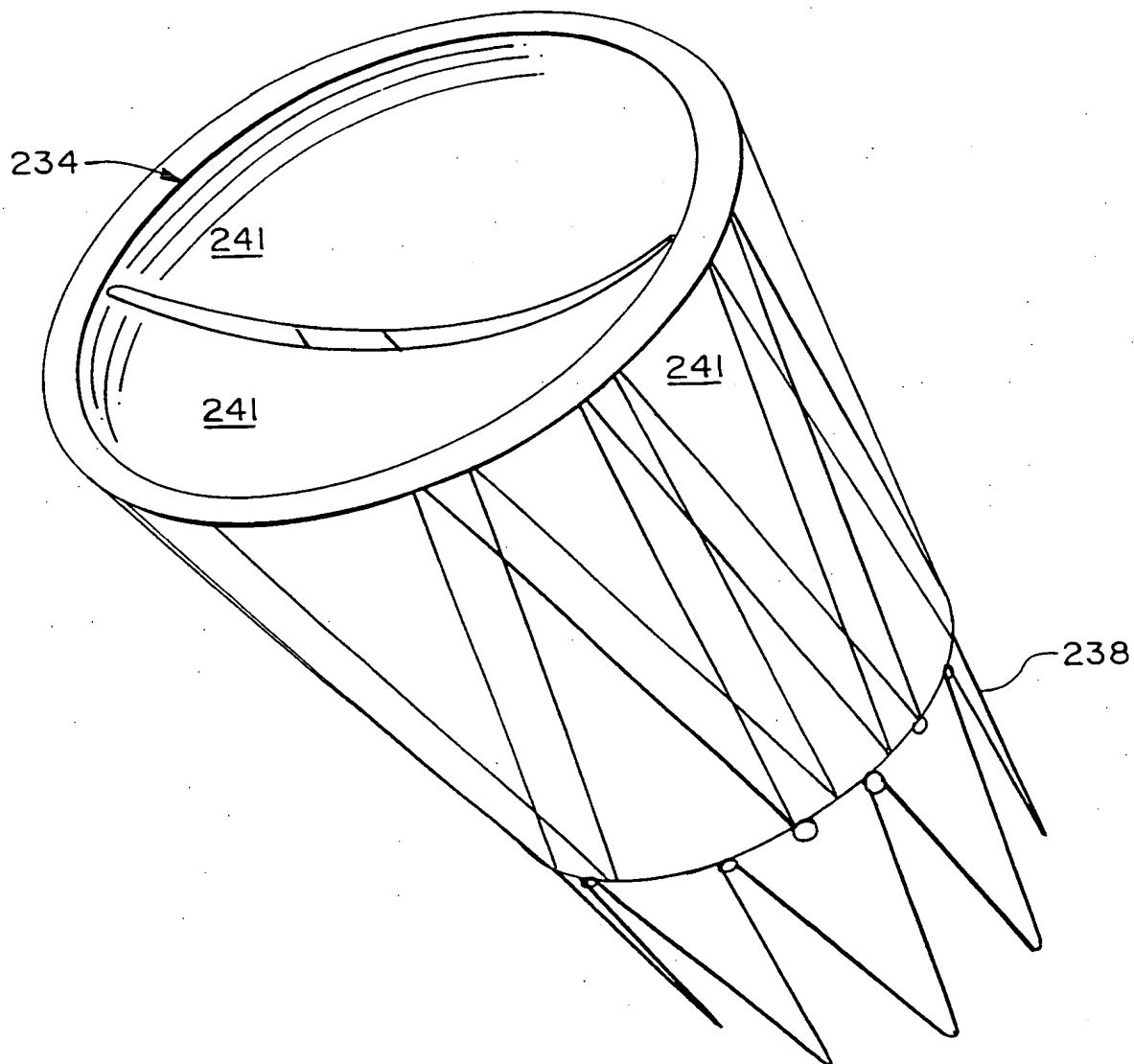


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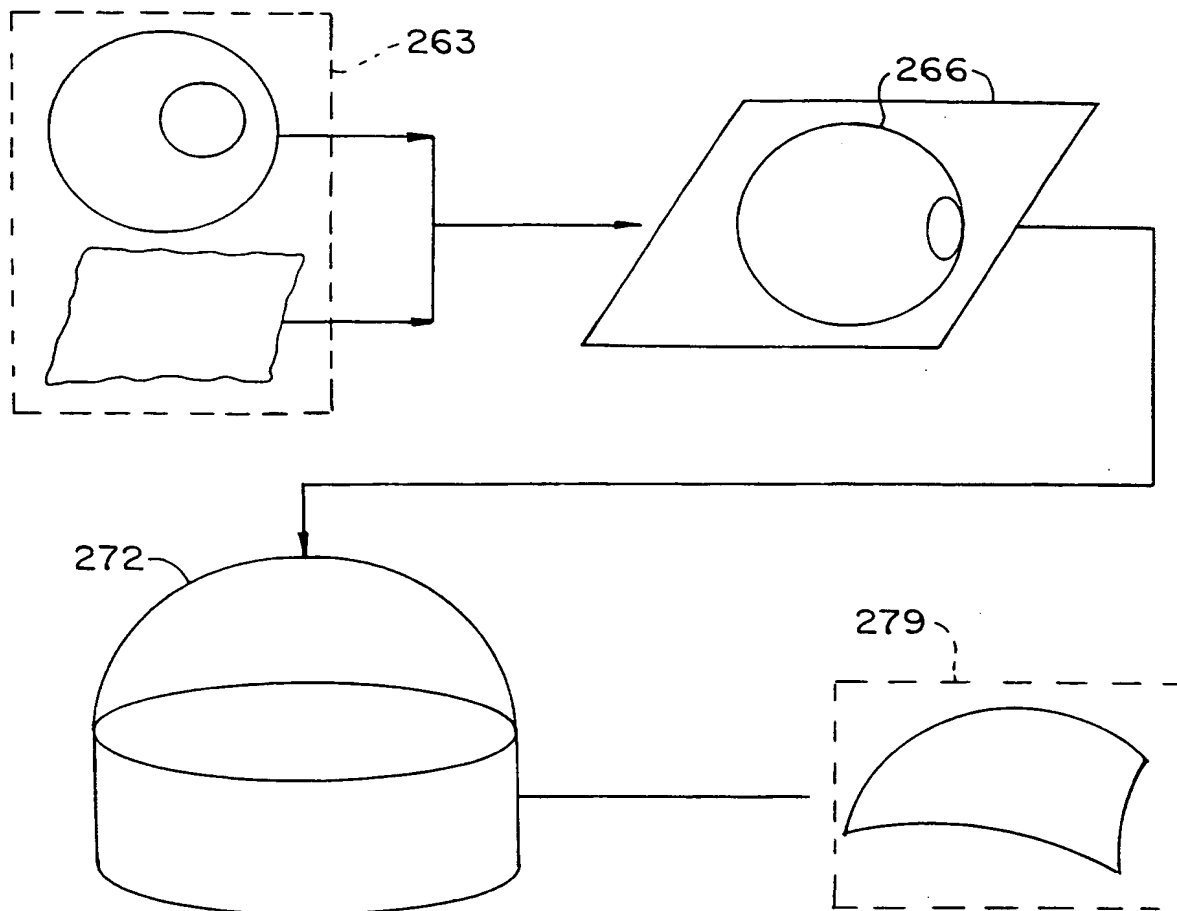
Fig. 23



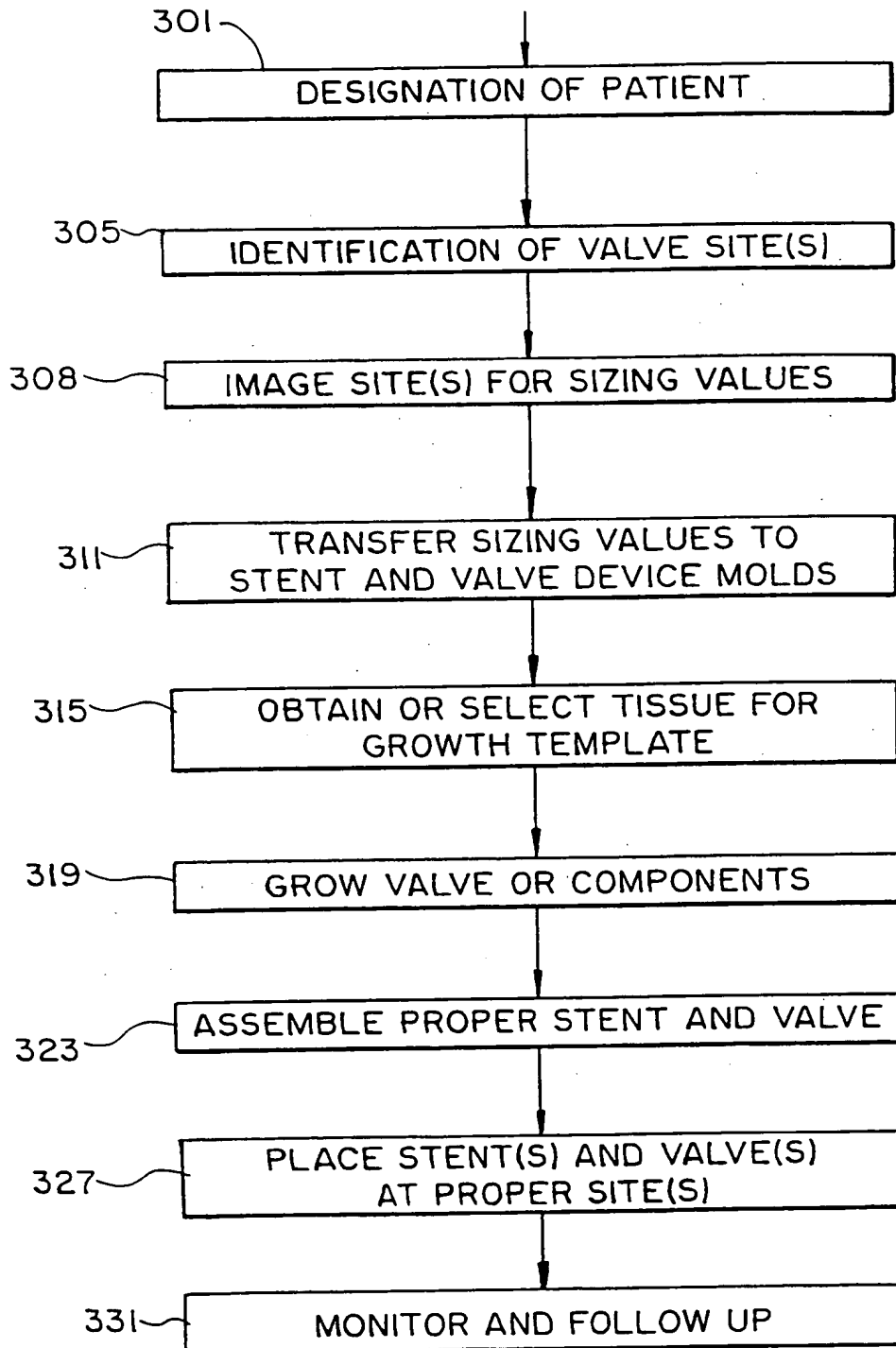
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Fig. 24

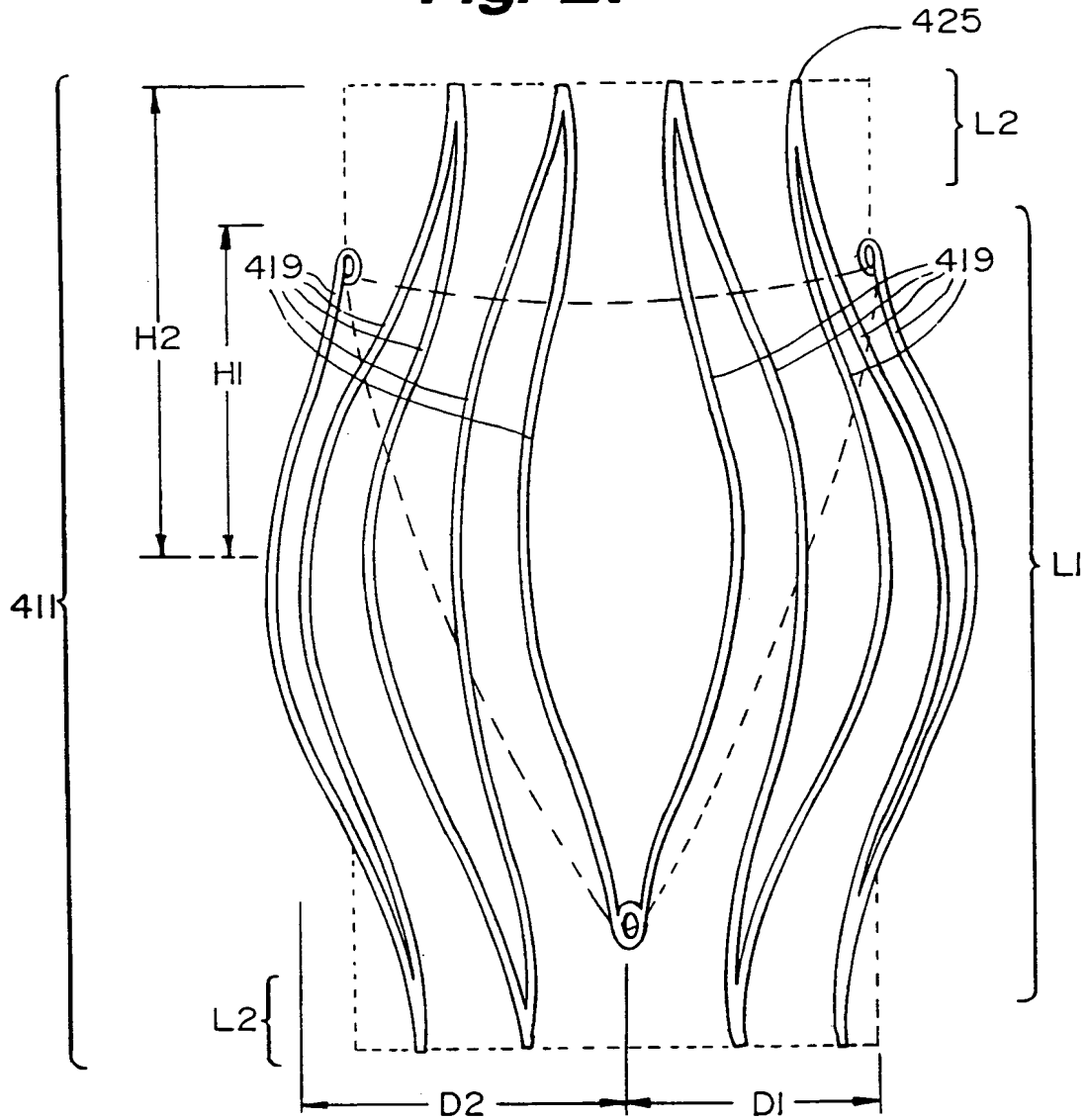
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Fig. 25

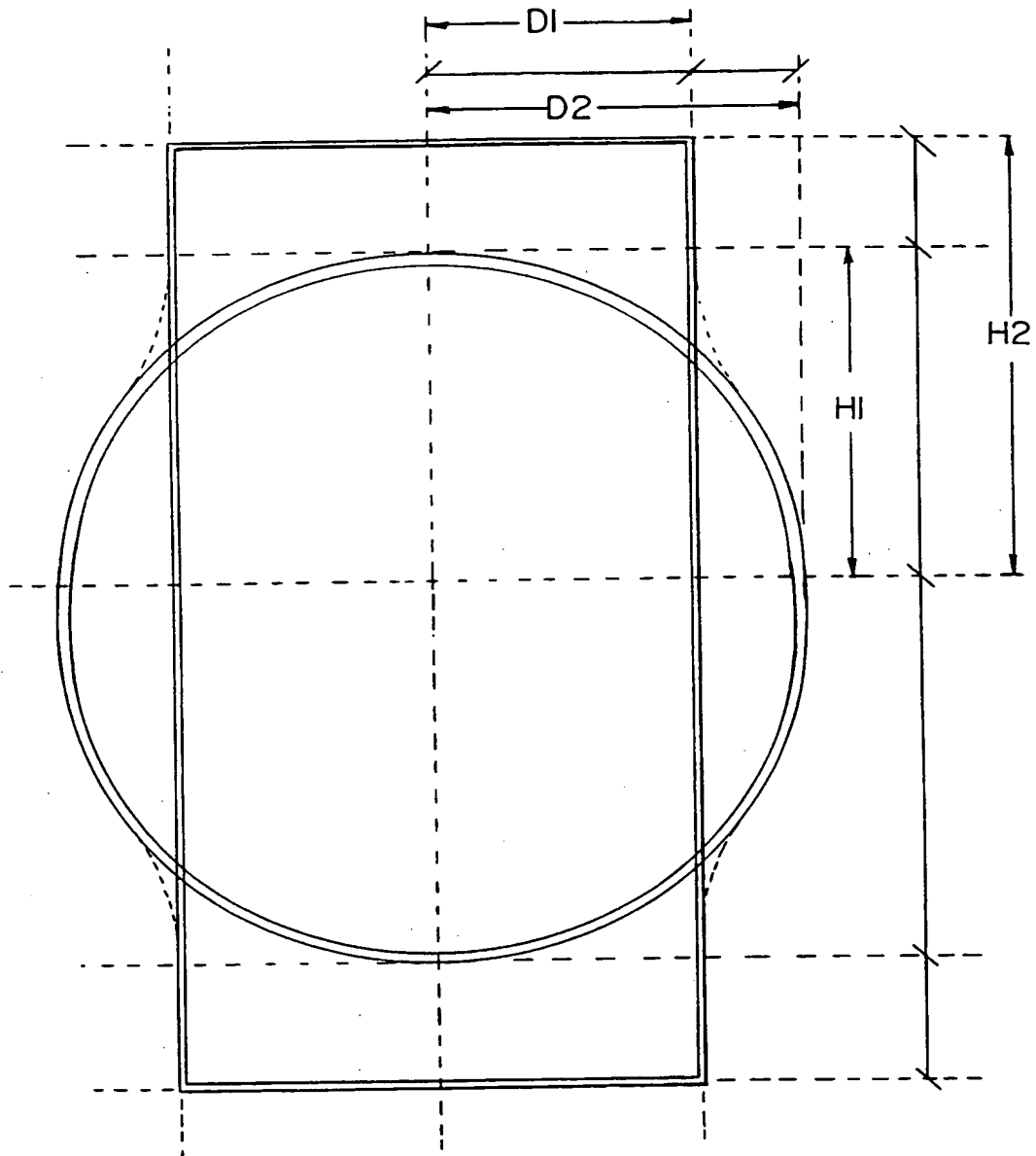
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Fig. 26

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Fig. 27

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Fig. 28

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/06974

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61F 2/24, 2/06

US CL : 623/1.15, 1.24, 2.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 623/1.15; 2.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A, E	US 6,221,091 B1 (Khosravi) 24 April 2001, col 1-8, figures 1-6	1-24
A, P	US 6,136,025 A (Barbut et al.) 24 October 2000, col. 1-10 and figures 1-6	1-24
Y	US 5,855,601 A (Bessler et al.) 05 January 1999, col. 1-12 and figures 1-16	1-24
Y	US 5,997,573 A (Quijano et al.) 07 December 1999, col. 1-14, and figures 1-21	1-24
Y	US 5,779,681 A (Bonn) 14 July 1998, col. 1-6 and figure 1	1-24
Y	US 5,549,666 A (Hata et al.) 27 August 1996, col. 1-12, and figures 1-5	1-24

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Date of the actual completion of the international search 16 MAY 2001	Date of mailing of the international search report 03 JUL 2001
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Suzette Jackson Telephone No. (703) 308-6516

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